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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/628,415	07/29/2003	Ludger Johannes	2121-0176P	6282

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EXAMINER	
MINNIFIELD, NITA M	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 04/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/628,415	JOHANNES ET AL.	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicants' amendment filed December 0, 2005 is acknowledged and has been entered. Claims 9-24 have been canceled. Claims 1-8 have been amended. Claims 1-8 are now pending in the present application. All rejections have been withdrawn in view of Applicants' comments, with the exception of those discussed below.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haicheur et al 2000 (J. Immunology, 2000, 165:3301-3308) in view of Wang et al (WO 95/11998).

Haicheur et al teaches a construct of the B subunit of Shiga toxin fused to a tumor peptide (abstract). The prior art teaches that the Shiga B subunit acts as a vector (i.e. carrier) (see abstract; p. 3301, col. 2). Haicheur et al teaches that the "Shiga B subunit targets this pathway in a receptor-dependent manner, namely via binding to the glycolipid Gb3. Because this receptor is highly expressed on various dendritic cells, it should allow preferential targeting of the Shiga B subunit to these professional APCs. Therefore, the Shiga B subunit appears to represent an attractive vector for vaccine development due to its ability to target dendritic cells and to induce specific CTL without the need for adjuvant." (abstract) Haicheur et al teaches that different peptides and proteins (i.e. OVA, SL8, P815A and P1A)

can be fused to the Shiga B subunit (materials and methods, p. 3302, col. 1). Haicheur et al teaches the STxB subunit and Z(n) wherein the Z can be a polypeptide (i.e. tumor peptide). The prior art does not teach the cysteine residues.

However, it is well known in the art to add cysteine residues to synthetic peptides for polymerization. Wang et al teaches that extra residues can be added to the ends of the SSAL (structured synthetic antigen libraries) and that KKK can be added at the amino terminus to increase peptide solubility, cysteine can be added to facilitate directed coupling to carrier molecules, and methionine can be added for cyanogen bromide cleavage if necessary. Wang et al teaches that the SSAL can be a domain within a peptide or can have other antigenic, diagnostic or therapeutic sites attached to it. The SSAL can be attached to a core sequence for facile delivery. These core sequences include branched cores, which can be an amino acid or an amino acid analog having two amino groups and one carboxyl group, each group capable of forming a peptide bond linkage. Preferably such amino acids are lysine or a lysine analog such as ornithine (see p. 20; p. 23). Wang et al teaches that "...SSAL can also be used to form conjugates, i.e., the SSAL, either in branched or linear form can be coupled directly or indirectly, by methods known in the art, to carrier proteins such as bovine serum albumin (BSA), human serum albumin (HSA), or to red blood cells or latex particles." (p. 21, lines 13-19) Since the prior art teaches that carriers (i.e. STxB, BSA, HSA etc) can be coupled directly or indirectly to a polypeptide and that the cysteine is added to facilitate coupling it would have been obvious to a person of ordinary skill in the art to combine to teachings of Haicheur et al in view of Wang et al to prepare a composition comprising the formula a STxB-polypeptide-cysteine (STxB-Z(n)-cys) for the purposes of targeting molecules to Gb3. The specification teaches that

B-subunit of *Shigella dysenteriae* is an homopentamer protein (5B--fragments) and is responsible for toxin binding to and internalization into target cells by interacting with the glycolipid Gb3 found on the plasma membranes of these cells (p. 1, l. 11-14), which is what the prior art teaches. The claimed invention is prima facie obvious in view of the combined teachings of Haicheur et al in view of Wang et al, absent any convincing evidence to the contrary.

Applicants have asserted that the Examiner has failed to properly support a rejection for prima facie obviousness and that there is no suggestion or motivation provided to modify Haicheur et al or to combine the reference teachings with Wang et al to establish prima facie obviousness. Applicants have asserted that Wang et al fails to contain any working examples or provide any results/data regarding the of use cysteine residue to facilitate directed binding of a peptide to a carrier and no carrier molecule is disclosed or discussed in Wang et al. More importantly, Wang et al fails to disclose or suggest the binding of a peptide, through a cysteine residue, to a carrier that will target the peptide to a specific pathway via receptor binding, such as is accomplished with the present invention and the Shiga B subunit. There is no suggestion or prediction in Wang et al as to whether construct containing the cysteine residue would still target to the desired pathway. Applicants have asserted that Wang et al. discloses that the cysteine residues may be added to either the N-terminus the C-terminus peptide to facilitate binding to the carrier. However, Wang et al fails to teach the site of the carrier where the cysteine residue bound to the peptide can be coupled so that the carrier function will not be impaired.

However, it is noted that the pending claims do not recite any limitations

with regard to "specific pathway" or "target to the desired pathway". Further, Wang et al, teaches that the cysteine can be added to facilitate directed coupling to carrier molecules. Because this concept is taught in the art, there is a reasonable expectation of success of making the claimed composition having the claimed formula, since Wang et al teaches that coupling the cysteine can be added to facilitate coupling to the carrier. Applicants and Haicheur et al use the STxB subunit for the same purpose of targeting molecules to Gb3. With regard to Applicants assertions regarding whether the cysteine is added to the N-terminus or C-terminus of the peptide, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to optimize the formula for the composition by using the terminus that provided a better universal polypeptidic carrier. It would have been obvious to one having ordinary skill in the art at the time the invention was made to couple the cysteine to the terminus (N- or C-) that does not alter the function of the carrier, since it has been held that discovering an optimum components of a composition are only routine skill in the art. *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980). The claimed invention is prima facie obvious in view of the combined teachings of Haicheur et al in view of Wang et al, absent any convincing evidence to the contrary.

The rejection is maintained for the reasons of record. Applicant's arguments filed December 2, 2005 have been fully considered but they are not persuasive. Applicants have asserted that the universal carrier of the present invention differs from those described in Wang et al by the process implemented to obtain the immunization. However, it is noted that the claimed invention is directed to a product, a carrier, not a process.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., size of the universal carrier) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In response to applicant's argument that Wang et al only has a brief single disclosure showing that cysteine residues can be added to synthetic peptides in order to facilitate the directed coupling of the peptides to the carrier. Applicants have asserted that the Examiner has focused only a single sentence of the reference and has ignored the rest of the teachings as a whole and that picking and choosing only those parts of a reference to render this rejection is contrary to the law. However, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, Wang et al teaches that cysteine residues can be used to facilitate binding of a peptide to a carrier. Wang et al teaches that cysteine can be added at the amino terminus of the protein to facilitate directed coupling to the carrier molecules (p. 20; see also p. 21).

The use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain." In re Heck, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983) (quoting In re Lemelson, 397 F.2d 1006, 1009, 158 USPQ 275, 277 (CCPA 1968)). A reference may be

relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Merck & Co. v. Biocraft Laboratories, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989). See also Celeritas Technologies Ltd. v. Rockwell International Corp., 150 F.3d 1354, 1361, 47 USPQ2d 1516, 1522-23 (Fed. Cir. 1998) (The court held that the prior art anticipated the claims even though it taught away from the claimed invention. "The fact that a modem with a single carrier data signal is shown to be less than optimal does not vitiate the fact that it is disclosed.").

Further, the rationale to modify or combine the prior art does not have to be expressly stated in the prior art; the rationale may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art, established scientific principles, or legal precedent established by prior case law. In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). See also In re Kotzab, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000) (setting forth test for implicit teachings); In re Eli Lilly & Co., 902 F.2d 943, 14 USPQ2d 1741 (Fed. Cir. 1990) (discussion of reliance on legal precedent); In re Nilssen, 851 F.2d 1401, 1403, 7 USPQ2d 1500, 1502 (Fed. Cir. 1988) (references do not have to explicitly suggest combining teachings); Ex parte Clapp, 227 USPQ 972 (Bd. Pat. App. & Inter. 1985) (examiner must present convincing line of reasoning supporting rejection); and Ex parte Levengood, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993) (reliance on logic and sound scientific reasoning).

4. No claims are allowed.

5. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

N. M. Minnifield
Primary Examiner
Art Unit 1645

NMM
April 6, 2006